IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 98-385-E)

In re Application of: Hauptmann et al.	)	
	)	
Serial No.: 09/525,998	)	Before the Examiner: E. O'Hara
	)	
Filed: March 15, 2000	)	Group Art Unit: 1646
	)	
For: TNF Receptors, TNF Binding	)	
Proteins and DNAs Coding	)	
For Them	)	

Commissioner for Patents
Washington, D.C. 20231

Madam:

RESPONSE TO RESTRICTION REQUIREMENT MAILED MARCH 13, 2002

Responsive to the Restriction Requirement, mailed March 13, 2002, Applicants elect to prosecute those claims directed to nucleic acid molecules comprising the nucleotide sequences set forth in SEQ ID NO: 1 and SEQ ID NO: 3, designated as Group A by the Examiner, with traverse. The basis for Applicants' traversal of the requirement is as follows.

Applicants respectfully submit that there will be no undue hardship on the Office in performing a search with respect to nucleic acid molecules comprising the nucleotide sequences set forth in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, and 19. A ClustalW multiple sequence alignment of the polypeptides encoded by these nucleotide sequences (*i.e.*, the amino acid sequences set forth in SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20) is shown in Exhibit A. The sequence alignment was performed using the application MacVector 7.1.1 (Accelrys, Cambridge, UK; http://www.accelrys.com) at the default settings. This sequence alignment indicates that there is a substantial degree of homology between the amino acid sequences set forth in SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20.
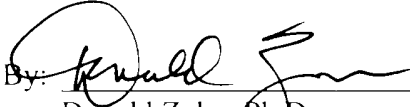
The nucleotide sequence set forth in SEQ ID NO: 1 encodes the TNF receptor protein (specification p. 3, ln. 30 to p. 4, ln. 25). The nucleotide sequence consisting of nucleotides 1

through 87 of SEQ ID NO: 1 (which is equivalent to the nucleotide sequence set forth in SEQ ID NO: 3) encodes a secretable TNF-binding protein (specification p. 4, ln. 27-41). As shown in Exhibit A, the polypeptides encoded by the nucleotide sequences set forth in SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19 all possess this portion of the TNF receptor protein. Moreover, this portion constitutes between 76.3% (SEQ ID NO: 8) and 99.4% (SEQ ID NO: 6) of the polypeptides encoded by the nucleotide sequences set forth in SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19. With the exception of an addition of ATG at the 5' end of the nucleotide sequences set forth in SEQ ID NOs: 5, 9, 15, and 19, the polypeptides encoded by the nucleotide sequences set forth in SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19 differ only by the presence or absence of sequences encoding the signal peptide (nucleotides 1 through 87 of SEQ ID NO: 1; specification p. 21, ln. 35 to p. 22, ln. 1), the portion of pro-protein cleaved following secretion (nucleotides 88 through 120 of SEQ ID NO: 1; specification p. 22, ln. 7-11), and the linker region (nucleotides 604 through 633 of SEQ ID NO: 1; specification p. 22, ln. 12-15) of TNF receptor protein. Applicants respectfully submit that there will be no undue hardship on the Office in performing a search with respect to the nucleotide sequences of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19, since a search for the elected nucleotide sequence set forth in SEQ ID NO: 3 will identify all of the non-elected sequences.

Applicants do not believe any additional fee is required. However, the Commissioner is authorized to charge any deficiency to Deposit Account No. 13-2490. If Examiner O'Hara believes it to be helpful, she is invited to contact the undersigned representative by telephone at (312) 913-0001.

<div align="right">

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

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Dated: <u>April 3, 2002</u>

By: Donald Zuhn, Ph.D.
Reg. No. 48,710

<div align="center">

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EXHIBIT A

ClustalW (v1.4) multiple sequence alignment

10 Sequences Aligned   Alignment Score   54899
Gaps Inserted   2   Conserved Identities   101

Pairwise Alignment Mode: Slow
Pairwise Alignment Parameters:
    Open Gap Penalty   10.0   Extend Gap Penalty   0.1
    Similarity Matrix: blosum

Multiple Alignment Parameters:
    Open Gap Penalty = 10.0   Extend Gap Penalty   0.0
    Delay Divergent = 40.   Gap Distance = 8
    Similarity Matrix: blosum

Processing time: 3.6 seconds

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SEQ  2     . MGLSTVPDLLLFLVLLELNGIYPSGVIGLVPHLGDREKRDVVPQCKYI    50
SEQ  4     :                                     DSVCPQCIYI    10
SEQ  6     :                                    MDSVCPQCIYI    11
SEQ  8     : MGLSTVPELLLFLVLLELNGIYPSGVIGLVPHLGDREKRDSVCPQCIYI    50
SEQ 10     :                            MLVPHLGDREKRDSVCPQCIYI    32
SEQ 12     : MGLSTVPELLLFLVLLELNGIYPSGVIG-----------DSVCPQCIYI    39
SEQ 14     : MGLSTVPELLLFLVLLELNGIYPSGVIGLVPHLGDREKRDSVCPQCIYI    50
SEQ 16     :                            MLVPHLGDREKRDSVCPQCIYI    32
SEQ 18     : MGLSTVPDLLLFLVLLELNGIYPSGVIG-----------DSVCPQCIYI    39
SEQ 20     :                                    MDSVCPQCIYI    11
                                               * * * * * * * * * *

SEQ  2    51 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL   100
SEQ  4    11 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL    60
SEQ  6    12 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL    61
SEQ  8    51 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL   100
SEQ 10    23 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL    72
SEQ 12    40 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL    89
SEQ 14    51 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL   100
SEQ 16    23 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL    72
SEQ 18    40 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL    89
SEQ 20    11 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL    61
             * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

SEQ  2   101 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL   150
SEQ  4    61 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL   110
SEQ  6    62 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL   111
SEQ  8   101 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL   150
SEQ 10    73 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL   122
SEQ 12    90 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL   139
SEQ 14   101 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL   150
SEQ 16    73 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL   122
SEQ 18    90 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL   139
SEQ 20    62 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL   111
             * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
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1

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SEQ  2   151  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTKLCLIQIE  200
SEQ  4   111  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTKLCLIQIE  160
SEQ  6   112  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTKLCLIQIE  161
SEQ  8   151  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTKLCLIQIE  200
SEQ 10   123  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTKLCLIQIE  172
SEQ 12   140  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTKLCLIQIE  189
SEQ 14   151  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTKLCLIQIE  200
SEQ 16   123  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTKLCLIQIE  172
SEQ 18   140  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTKLCLIQIE  189
SEQ 20   112  NGTVHLSCQEFQNTVCTCHAGFFLRENECVSCSNCHESLECTKLCLIQIE  161
              *************************************************

SEQ  1   201  NVFGTEDSGTTVLLILVIFFGLCLLSLLFIGLMYRYQRWKSKLYSIVCGK  250
SEQ  4   161  N                                                  161
SEQ  6   162  N                                                  162
SEQ  8   201  NVFGTEDSGTT                                        211
SEQ 10   172  NVFGTEDSGTT                                        182
SEQ 12   190  NVFGTEDSGTT                                        200
SEQ 14   201  N                                                  201
SEQ 16   172  N                                                  172
SEQ 18   190  N                                                  190
SEQ 20   161  NVFGTEDSGTT                                        171
              *

SEQ  2   251  STPEKEGELEGTTTKPLAPNPSFSPTPGFTPTLGFSPVPSSTFTSSSTYT  300
SEQ  4   161                                                     161
SEQ  6   163                                                     163
SEQ  8   212                                                     211
SEQ 10   184                                                     184
SEQ 12   201                                                     200
SEQ 14   202                                                     201
SEQ 16   173                                                     173
SEQ 18   191                                                     190
SEQ 20   172                                                     172

SEQ  2   301  PGDCPNFAAPEREVAPPYQGADPILATALASDPIPNPLQKWEDSAHKPQS  350
SEQ  4   161                                                     161
SEQ  6   163                                                     163
SEQ  8   211                                                     211
SEQ 10   184                                                     184
SEQ 12   201                                                     200
SEQ 14   201                                                     201
SEQ 16   173                                                     173
SEQ 18   191                                                     190
SEQ 20   173                                                     172
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SEQ 2    351  LDTDDPATLYAVVENVPPLRWKEFVRRLGLSDHEIDRLELQNGRCLREAQ  400
SEQ 4    162                                                       161
SEQ 6    163                                                       162
SEQ 8    212                                                       211
SEQ 10   184                                                       183
SEQ 12   201                                                       200
SEQ 14   202                                                       201
SEQ 16   174                                                       173
SEQ 18   191                                                       190
SEQ 20   173                                                       172


SEQ 2    401  YSMLATWRRRTPRREATLELLGRVLRDMDLLGCLEDIEEALCGPAALEIA  450
SEQ 4    162                                                       161
SEQ 6    163                                                       162
SEQ 8    212                                                       211
SEQ 10   184                                                       183
SEQ 12   201                                                       200
SEQ 14   202                                                       201
SEQ 16   174                                                       173
SEQ 18   191                                                       190
SEQ 20   173                                                       172


SEQ 2    451  PSLLR  455
SEQ 4    162         161
SEQ 6    163         162
SEQ 8    212         211
SEQ 10   184         183
SEQ 12   201         200
SEQ 14   202         201
SEQ 16   174         173
SEQ 18   191         190
SEQ 20   173         172
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